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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/528,682	03/20/2000	Mariagrazia Pizza	0342.105	5794

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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 11/15/2001

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/528,682

Applicant(s)

Pizza et al.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sep 10, 2001
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-29 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3 20) ☐ Other:

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DETAILED ACTION

Status of the claims

1. Response to restriction requirement filed 9/10/01 is acknowledged. Applicant's traverse is deemed persuasive and the restriction requirement is withdrawn. Claims 7-29 are examined.

Information Disclosure Statement

2. Applicants' Information Disclosure Statement filed 8/8/2000 has been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

Abstract

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Drawings

4. The drawings are objected because of the defects noted on the PTO-948.

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Claim Rejections - 35 U.S.C. § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 7-29 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The claims are drawn to polynucleotides encoding a sequence of subunit A of E.Coli toxin, LT-A, wherein Ala residue at position 72 is replaced with Arg residue; further, the claims are drawn to corresponding vectors and host cells. As there is a plurality of LT-A proteins and only proteins having a replaced Ala residue in position 72 are subject of invention, the presence of Ala/Arg in position 72 is critical and essential to the practice of the invention. However, no particular LT-A having sequence with Ala or Arg in the indicated position 72 is included in the claims or enabled by the disclosure. Multiple descriptions in the prior art cited in the specification refer to plurality of products, not necessarily comprising Ala⁷². For example, specification, p. 5, line 25 +, describes LT-A proteins having not Ala⁷², but a residue "which corresponds to Ala⁷²". However, no particular LT-A having sequence with Ala in the indicated position is included in the claims or is present in the specification. Accordingly, the claims and the specification lack the essential subject matter. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

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There is no incorporation by reference of any particular sequence. Even if there was an attempt to incorporate a sequence by reference, it would have been improper as MPEP 608(p) clearly defines that

"Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference.

6. Claims 7-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The claims are drawn, in part, to polynucleotides encoding immunogenic fragments of LT-A comprising at least five residues. There is no description in the claims or specification describing said fragments in such detail that will sufficiently identify the epitope sequence required for the fragment to retain immunogenic properties.

Claim Rejections - 35 USC § 102 and 103.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States...

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 7,11,15 are rejected under 35 U.S.C. 102(b) as clearly anticipated by Domenighini et al (WO 93/13202).

Domenighini describes a polynucleotide encoding LT-A subunit having Ala at position 72 substituted with Arg residue and corresponding vector and expression cells. See p.46, line 51, and page 45.

8. Claims 7-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 145486.

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The patent teaches compositions and vaccines comprising modified LT-A of the following original sequences, respectively:

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1 MKNITFIFFI LLASPLYANG DRLYRADSRP PDEIKRSGGL MPRGHNEYFD
51 RGTQMNINLY DHARGTETTGF VRYDDGYVST SLSLRSAHLA GQFILSGYST
101 YYIYVIATAP NMFNVNDVLG VYSPHPYEQE VSALGGIPYS QIYGWYRVNF
151 GVIDERLHRN REYDRYYRN LNIAPAEDGY RLAGFPPDHQ AWREEPWIHH
201 APQGCN SSR TITGDT CNEE TQNLSTIYLR EYQSKVKRQI FSDYQSQVDI
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The referenced protein comprises sequence TGFVRYDDG (underlined), which is a fragment of subunit LT-A having Arg residue instead of Ala. As the referenced protein presents a practical interest, as it can be used as an immunogenic stimulant and vaccine, one would be motivated to produce such protein recombinantly using conventional methods of molecular biology. Further, in regard to the second immunogenic component, because combination therapies for generation of immune response are well-known in the art and because it would have been desirable to use plural therapies in order to maximize the effectiveness of the treatment, it would be *prima facie* obvious to one of ordinary skills in the art at the time the invention was made to be motivated to use the immunogenic subunit LT-A in combination with another immunogenic antigen. Modification to combine components all known to be useful as immunogenic agents would have been obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be useful for the very same purpose. Consequently, it would have been obvious to produce such conjugate protein recombinantly using conventional methods of molecular biology.

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Conclusion.

9. No claims are allowed

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

November 12, 2001

mlb

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

